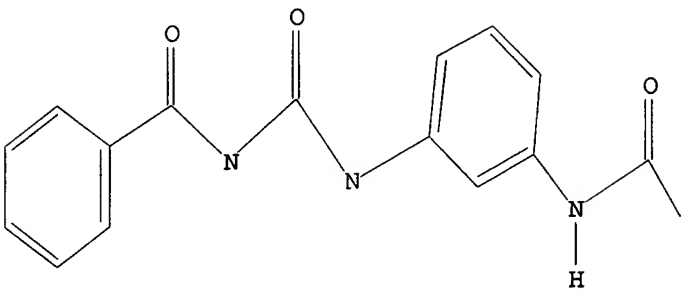
```
=> d his

     (FILE 'HOME' ENTERED AT 15:53:49 ON 20 JUN 2006)

     FILE 'REGISTRY' ENTERED AT 15:54:03 ON 20 JUN 2006
L1              STRUCTURE UPLOADED
L2            1 S L1
L3            9 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 15:54:45 ON 20 JUN 2006
L4            2 S L3

     FILE 'HCAPLUS, HCAOLD, USPATFULL, EPFULL, BIOSIS' ENTERED AT 15:56:01 ON
     20 JUN 2006
L5         7852 S ?PHENYL UREA OR ACYL PHENYL UREA?
L6          873 S L5 AND (DIABETES OR BLOOD SUGAR OR BLOOD GLUCOSE OR HYPOGLYC
L7          858 S L6 AND (PHARMACEUTICAL OR TREAT? OR COMPOSITION)
L8            1 S L7 AND ACYLPHENYLUREA
```

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 15:54:21 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 27 TO ITERATE

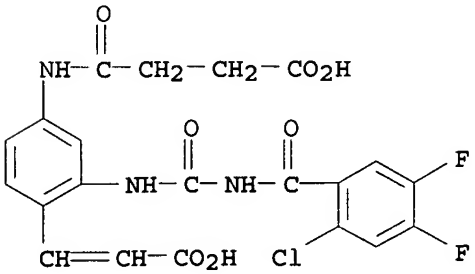
100.0% PROCESSED 27 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 229 TO 851
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> d scan

L2 1 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Butanoic acid, 4-[[4-(2-carboxyethenyl)-3-[[[(2-chloro-4,5-difluorobenzoyl)amino]carbonyl]amino]phenyl]amino]-4-oxo- (9CI)
MF C21 H16 Cl F2 N3 O7



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

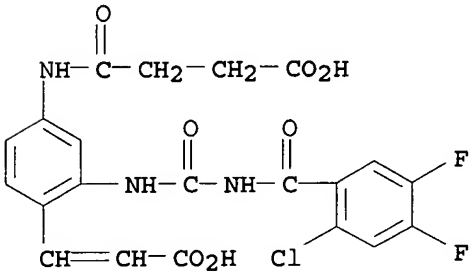
=> s l1 full
FULL SEARCH INITIATED 15:54:29 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 397 TO ITERATE

100.0% PROCESSED 397 ITERATIONS 9 ANSWERS
SEARCH TIME: 00.00.01

L3 9 SEA SSS FUL L1

=> d scan

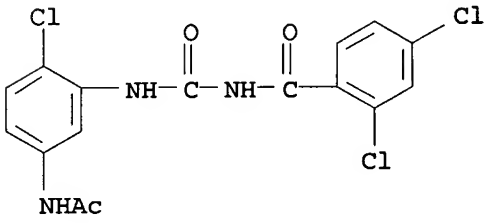
L3 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Butanoic acid, 4-[[4-(2-carboxyethenyl)-3-[[[(2-chloro-4,5-difluorobenzoyl)amino]carbonyl]amino]phenyl]amino]-4-oxo- (9CI)
MF C21 H16 Cl F2 N3 O7



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

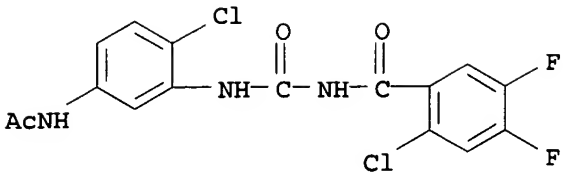
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):5

L3 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Benzamide, N-[[[5-(acetylamino)-2-chlorophenyl]amino]carbonyl]-2,4-dichloro- (9CI)
MF C16 H12 Cl3 N3 O3



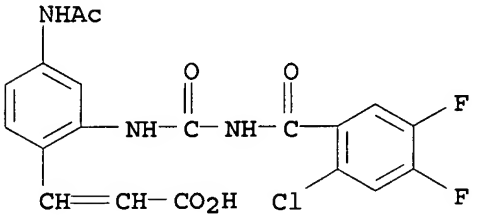
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN Benzamide, N-[[[5-(acetylamino)-2-chlorophenyl]amino]carbonyl]-2-chloro-4,5-difluoro- (9CI)
MF C16 H11 Cl2 F2 N3 O3



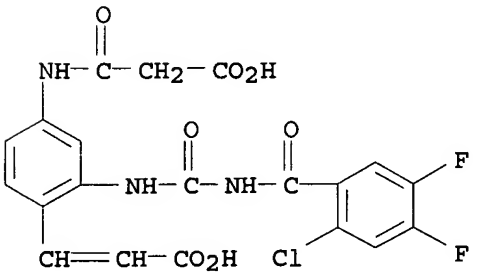
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 2-Propenoic acid, 3-[4-(acetylamino)-2-[[[(2-chloro-4,5-difluorobenzoyl)amino]carbonyl]amino]phenyl]- (9CI)
MF C19 H14 Cl F2 N3 O5



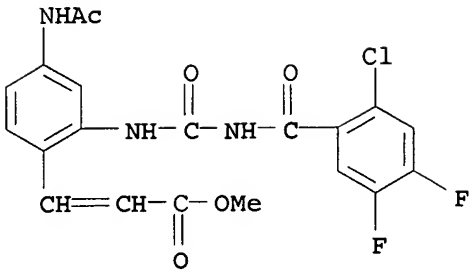
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 2-Propenoic acid, 3-[4-[(carboxyacetyl)amino]-2-[[[(2-chloro-4,5-difluorobenzoyl)amino]carbonyl]amino]phenyl]- (9CI)
MF C20 H14 Cl F2 N3 O7



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 9 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 2-Propenoic acid, 3-[4-(acetylamino)-2-[[[(2-chloro-4,5-difluorobenzoyl)amino]carbonyl]amino]phenyl]-, methyl ester (9CI)
MF C20 H16 Cl F2 N3 O5



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file hcaplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	166.94	167.15

FILE 'HCAPLUS' ENTERED AT 15:54:45 ON 20 JUN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 20 Jun 2006 VOL 144 ISS 26
FILE LAST UPDATED: 19 Jun 2006 (20060619/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 2 L3

=> d 1-2 ibib abs hitstr

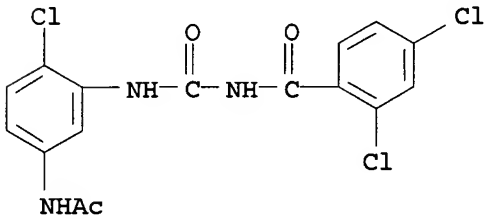
L4 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:980048 HCAPLUS
DOCUMENT NUMBER: 143:359432
TITLE: Acyl Ureas as Human Liver Glycogen Phosphorylase Inhibitors for the Treatment of Type 2 Diabetes
AUTHOR(S): Klabunde, Thomas; Wendt, K. Ulrich; Kadereit, Dieter;

Brachvogel, Volker; Burger, Hans-Joerg; Herling, Andreas W.; Oikonomakos, Nikos G.; Kosmopoulou, Magda N.; Schmoll, Dieter; Sarubbi, Edoardo; Von Roedern, Erich; Schoenafinger, Karl; Defossa, Elisabeth
CORPORATE SOURCE: Scientific and Medical Affairs, Sanofi-Aventis Deutschland GmbH, Frankfurt am Main, D-65926, Germany
SOURCE: Journal of Medicinal Chemistry (2005), 48(20), 6178-6193
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:359432

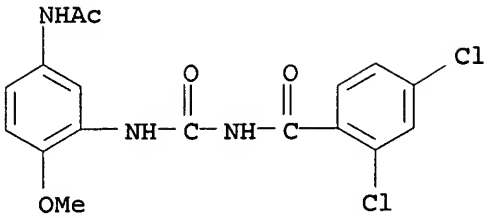
AB Using a focused screening approach, acyl ureas have been discovered as a new class of inhibitors of human liver glycogen phosphorylase (hlGPa). The x-ray structure of screening hit 1 (IC50 = 2 μM) in a complex with rabbit muscle glycogen phosphorylase b reveals that 1 binds at the AMP site, the main allosteric effector site of the dimeric enzyme. A first cycle of chemical optimization supported by x-ray structural data yielded derivative 21, which inhibited hlGPa with an IC50 of 23±1 nM, but showed only moderate cellular activity in isolated rat hepatocytes (IC50 = 6.2 μM). Further optimization was guided by (i) a 3D pharmacophore model that was derived from a training set of 24 compds. and revealed the key chemical features for the biol. activity and (ii) the 1.9 Å crystal structure of 21 in complex with hlGPa. A second set of compds. was synthesized and led to 42 with improved cellular activity (hlGPa IC50 = 53±1 nM; hepatocyte IC50 = 380 nM). Administration of 42 to anesthetized Wistar rats caused a significant reduction of the glucagon-induced hyperglycemic peak. These findings are consistent with the inhibition of hepatic glycogenolysis and support the use of acyl ureas for the treatment of type 2 diabetes.

IT **866329-41-1P 866329-42-2P 866329-44-4P 866329-45-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(acyl ureas as human liver glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

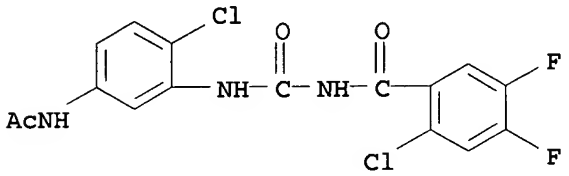
RN 866329-41-1 HCAPLUS
CN Benzamide, N-[[[5-(acetylamino)-2-chlorophenyl]amino]carbonyl]-2,4-dichloro- (9CI) (CA INDEX NAME)



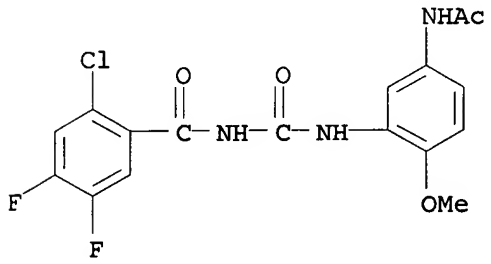
RN 866329-42-2 HCAPLUS
CN Benzamide, N-[[[5-(acetylamino)-2-methoxyphenyl]amino]carbonyl]-2,4-dichloro- (9CI) (CA INDEX NAME)



RN 866329-44-4 HCAPLUS
CN Benzamide, N-[[[5-(acetylamino)-2-chlorophenyl]amino]carbonyl]-2-chloro-4,5-difluoro- (9CI) (CA INDEX NAME)



RN 866329-45-5 HCAPLUS
CN Benzamide, N-[[[5-(acetylamino)-2-methoxyphenyl]amino]carbonyl]-2-chloro-4,5-difluoro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:991475 HCAPLUS
DOCUMENT NUMBER: 140:41915
TITLE: Preparation of N-benzoylureidophenylacrylic acids as antidiabetic agents
INVENTOR(S): Schoenafinger, Karl; Defossa, Elisabeth; Kadereit, Dieter; Von Roedern, Erich; Klabunde, Thomas; Burger, Hans-Joerg; Herling, Andreas; Wendt, Karl-Ulrich
PATENT ASSIGNEE(S): Aventis Pharma Deutschland G.m.b.H., Germany
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003104188	A1	20031218	WO 2003-EP5355	20030522

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10225635	C1	20031224	DE 2002-10225635		20020607
CA 2488760	AA	20031218	CA 2003-2488760		20030522
AU 2003238373	A1	20031222	AU 2003-238373		20030522
BR 2003011646	A	20050315	BR 2003-11646		20030522
EP 1513800	A1	20050316	EP 2003-732438		20030522
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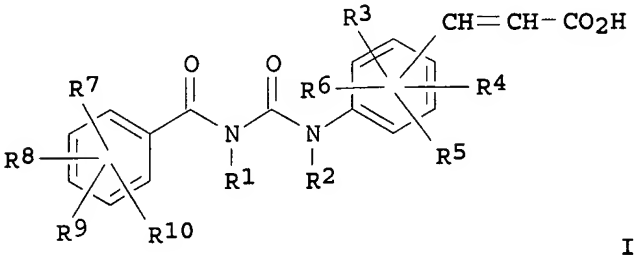
CN 1659137	A	20050824	CN 2003-813173		20030522
JP 2005529164	T2	20050929	JP 2004-511258		20030522
US 2004102518	A1	20040527	US 2003-456570		20030606
US 7049341	B2	20060523			
NO 2005000087	A	20050106	NO 2005-87		20050106
PRIORITY APPLN. INFO.:			DE 2002-10225635	A	20020607
			US 2002-411982P	P	20020919
			WO 2003-EP5355	W	20030522

OTHER SOURCE(S): MARPAT 140:41915

GI



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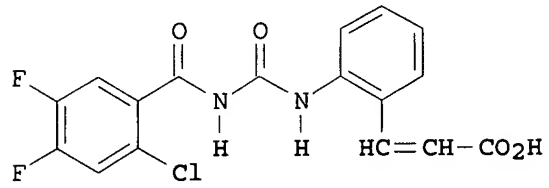


II

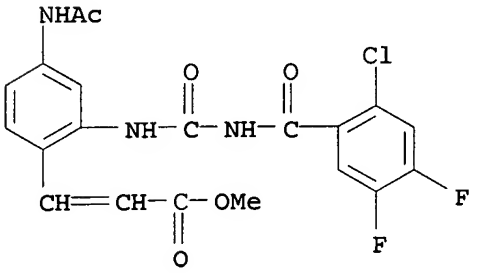
AB Title compds. I [R7, R8, R9, R10 = H, halo, OH, etc.; R1, R2 = H, (un)substituted alkyl, e.g., OH, O-alkyl, NH2, etc.; R3, R4, R5, R6 = H, halo, NO2, etc.; R11 = OR12, NR18R19; R12 = H, alkyl, alkenyl, etc.; R18, R19 = H, alkyl, alkenyl, etc.;] and their pharmaceutically acceptable salts were prepared For example, condensation of 2-chloro-4,5-difluorobenzoylisocyanate, e.g., prepared from 2-chloro-4,5-difluorobenzamide and oxalyl chloride, and 3-(2-aminophenyl)acrylic acid afforded N-benzoylureidocinnamate II in 76% yield. In glycogen phosphorylase-A inhibition assays, 14-examples of compds. I at 10 μM exhibited 83->100% inhibition (sic),. Compds. I are claimed useful as as antidiabetic agents.

IT **634616-74-3P**

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic

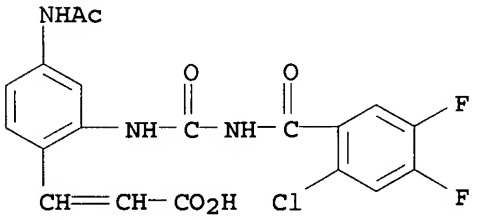
preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(target compound; preparation of N-benzoylureidophenylacrylic acids as antidiabetic agents)

RN 634616-74-3 HCAPLUS
CN 2-Propenoic acid, 3-[4-(acetylamino)-2-[[[(2-chloro-4,5-difluorobenzoyl)amino]carbonyl]amino]phenyl]-, methyl ester (9CI) (CA INDEX NAME)

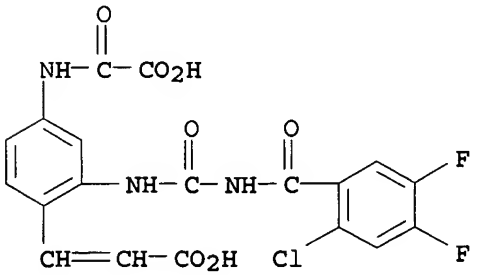


IT **634616-62-9P 634616-63-0P 634616-64-1P 634616-65-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of N-benzoylureidophenylacrylic acids as antidiabetic agents)

RN 634616-62-9 HCAPLUS
CN 2-Propenoic acid, 3-[4-(acetylamino)-2-[[[(2-chloro-4,5-difluorobenzoyl)amino]carbonyl]amino]phenyl]- (9CI) (CA INDEX NAME)

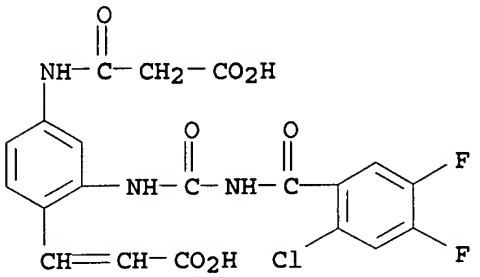


RN 634616-63-0 HCAPLUS
CN 2-Propenoic acid, 3-[4-[(carboxycarbonyl)amino]-2-[[[(2-chloro-4,5-difluorobenzoyl)amino]carbonyl]amino]phenyl]- (9CI) (CA INDEX NAME)



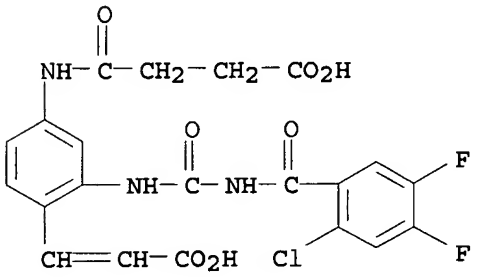
RN 634616-64-1 HCAPLUS

CN 2-Propenoic acid, 3-[4-[(carboxyacetyl)amino]-2-[[[(2-chloro-4,5-difluorobenzoyl)amino]carbonyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RN 634616-65-2 HCAPLUS

CN Butanoic acid, 4-[[4-(2-carboxyethenyl)-3-[[[(2-chloro-4,5-difluorobenzoyl)amino]carbonyl]amino]phenyl]amino]-4-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT